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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/532,831	03/09/2006	Hans-Ulrich Petereit	267336US0PCT	8866

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OBLON, SPIVAK, MCCLELLAND MAIER & NEUSTADT, L.L.P.
1940 DUKE STREET
ALEXANDRIA, VA 22314

EXAMINER	
WESTERBERG, NISSA M	
ART UNIT	PAPER NUMBER
1618	

NOTIFICATION DATE	DELIVERY MODE
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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Notice of the Office communication was sent electronically on above-indicated "Notification Date" to the following e-mail address(es):

patentdocket@oblon.com
oblonpat@oblon.com
jgardner@oblon.com

Office Action Summary	Application No.	Applicant(s)	
	10/532,831	PETEREIT ET AL.	
	Examiner	Art Unit	
	Nissa M. Westerberg	1618	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *23 July 2009*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1 - 3, 8 - 11, 13, 14, 16* is/are pending in the application.

4a) Of the above claim(s) *10 and 11* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1 - 3, 8, 9, 13, 14, 16* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *7/23/09*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Applicants' arguments, filed July 23, 2009, have been fully considered but they are not deemed to be fully persuasive. The following rejections and/or objections constitute the complete set presently being applied to the instant application.

Claim Rejections - 35 USC § 103

1. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

2. The factual inquiries set forth in *Graham* **v.** *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

3. This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation

under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

4. Claims 1 – 3, 8, 9, 13, 14 and 16 were rejected under 35 U.S.C. 103(a) as being unpatentable over Ulmius et al. (US 5,643,602) in view of Beckert et al. (WO 01/68058, citations from the English equivalent US 2002/019228). This rejection is MAINTAINED for the reasons of record set forth in the Office Actions mailed October 1, 2008 and April 24, 2009 and those set forth below.

Applicant traverses this rejection on the grounds that the Office commits a clear legal error by dismissing a showing of unexpected results. While not conceding that a skilled person would choose EUDRAGIT® NE for the inner matrix from Ulmius and the outer coating of EUDRAGIT® FS from Beckert, one skilled in the art would never expect the “hypotonic/isotonic" effect that has been so clearly demonstrated for the claimed invention. This advantage is also not predictable. It is advantageous to omit plasticizers in the inner coating since it is always attempted to reduce excipients wherever possible to avoid or reduce interactions or incompatibilities with the active ingredient. This is only possible when EUDRAGIT® NE polymers are used and acceptable results are not achieved with EUDRAGIT® RL even when a plasticizer is used. The choice of EUDRAGIT® NE polymers is important to achieve this ability and is not at all suggested by the cited art. Ulmius uses plasticizers throughout the examples and EUDRAGIT® NE

and EUDRAGIT® RL, the latter not working as shown in figure 6 of the instant application. EUDRAGIT® NE is not used as the inner coating in a single example of Ulmius. Beckert teaches away from the present invention because the pharmaceutically active substance is placed onto the neutral core and not bound in the inner coating material as claimed. There is not a reasonable prediction of success from the teachings of cited art for the percentage release of the active substances as defined by claim 1 because the evidence shows that combinations within the teachings of Ulmius lead to compositions not meeting the definition. Examples 5 and 6 used EUDRAGIT® NE 30 D and EUDRAGIT® RL 30D as inner coatings respectively with EUDRAGIT® L 30 D as the outer gastroresistant coating in both examples. The release profiles are shown in figures 5 and 6 respectively, wherein only the composition of example 5 shows a release profile as recited in claim 1.

These arguments are unpersuasive. In order to overcome a prima facie case of obviousness, it is incumbent upon the Applicant to provide comparative test evidence that demonstrates unexpected superiority of the claimed compositions versus the closest prior art compositions, and not simply an advantage predictable from the prior art. See *In re Chapman*, 148 USPQ 711, 715 (CCPA, 1966). Moreover, such proffered comparisons must be commensurate in scope with the breadth of the claims. See *In re Clemens*, 206 USPQ 289, 296 (CCPA, 1980) and *In re Coleman*, 205 USPQ 1172, 1175 (CCPA 1980). As Applicant has explained, both of the coatings in examples 5 and 6 use EUDRAGIT® L 30 D as the outer coating. EUDRAGIT® L 30 D is a copolymer of 50% by weight ethyl acrylate and 50% by weight methacrylic acid (¶ [0140] of the

PGPub for the instant application) and does not fall within the scope of the multilayer dosage form recited in claim 1. The composition recited for the outer coating in claim 1 appears to be EUDRAGIT® FS (¶ [0106] of instant specification). As the composition for which data is shown is not encompassed the instant claims, the allegations of unexpected results are not persuasive.

Additionally, there are more differences between example 5 and 6 other than the polymer of the inner coating. The inner coating of example 5 only contains polymer, budesonide as the active ingredient and water whereas the inner coating of example 6 contains polymer, talc and the plasticizer triethyl citrate (TEC) and the aminosalicyclic acid ingredient appears to be in the core (¶¶ [0155] – [0156]). The change in behavior between the release profiles in figures 5 and 6 may not simply be due to the differences in inner polymer coating layer, but the other differences in the formulation.

Applicants have not presented any evidence that the combination of EUDRAGIT® NE with EUDRAGIT® FS is the only combination that possesses this property. A variety of combinations of inner and outer EUDRAGIT® layers taught by Ulmius alone or in combination with Beckert. Without additional evidence, what is expected and what is unexpected cannot be determined. If all other combinations of EUDRAGIT® polymers do not possess that “hypotonic/isotonic" effect relied upon by Applicant, then the results may be unexpected, but based on the two examples provided and the multiple differences in the formulation between those examples, such a conclusion cannot be drawn at this time. Applicants’ arguments without factual support are mere allegations and cannot be found persuasive. Applicant have also not

presented evidence EUDRAGIT® NE 30 D is the only polymer for the inner layer that can be used without a plasticizer.

Disclosed examples and preferred embodiments do not constitute a teaching away from a broader disclosure or nonpreferred embodiments. *In re Susi*, 440 F.2d 442, 169 USPQ 423 (CCPA 1971). (MPEP 2123). Furthermore, "the prior art's mere disclosure of more than one alternative does not constitute a teaching away from any of these alternatives because such disclosure does not criticize, discredit, or otherwise discourage the solution claimed…." *In re Fulton*, 391 F.3d 1195, 1201, 73 USPQ2d 1141, 1146 (Fed. Cir. 2004). **MPEP 2123**, emphasis added. Ulmius discloses that the coatings may optionally comprise plasticizers (col 5, ln 48 – 50). Based on this teaching, one of ordinary skill in the art would know that while plasticizers are not essential ingredients, they may be included if the situation requires. In Ulmius et al., the inner polymer coating layer contains the active ingredient while in Beckert et al., the active ingredient is found in the core. Merely because the two references locate the active ingredient in two different locations does not teach away from one arrangement over the other as there is no criticism, discrediting or discouragement of the other alternative.

5. Claims 1 – 3, 8, 9, 13, 14 and 16 are rejected under 35 U.S.C. 103(a) as being unpatentable over Ulmius et al. (US 5,643,602) in view of Gang et al. (Proceedings of the 7th SECJ, 2001; cited on IDS submitted July 23, 2009).

Ulmius discloses multilayer compositions of corticosteroids such as budesonide (col 3, ln 6; col 4, ln 50). Each unit comprises a core and two layers on that core (col 5,

ln 3 – 4). The core can either be formulated with the glucocorticosteroid homogenously throughout the core or the active ingredient can be applied to the exterior of the seed (col 5, ln 5 – 8). When the drug is applied to the seed, the drug is applied in combination with a polymer that acts as a binder for the active ingredient and to limit the release rate (col 5, ln 12 – 16). Preferred film-forming polymers are ethylcellulose or copolymers of acrylic and methacrylic acid esters such as the compounds sold under the tradenames EUDRAGIT® NE, EUDRAGIT® RL and EUDRAGIT® RS (col 5, ln 24 – 26). EUDRAGIT® NE 30D is a polymer that meets the monomer requirements for the inner coating in claims 1 and 2 as it contains 65 wt% ethyl acrylate and 35% wt% methyl methacrylate (p 26, ln 10 – 12 of the instant application). The ratio of the active ingredient to the polymer is 1:6.6 and 1:2.4 examples 1 and 2 respectively (col 8, ln 24 – 30; col 9, ln 14 – 20). The film-forming temperature of the polymer is determined by the composition of the polymer and as the composition of the polymers are the same, the film-forming temperature of the polymer will meet the limitations set forth in the claim. The release profile of the active ingredient should be such that no release occurs in the stomach but is released in either the small intestine or caecum (col 4, ln 34 – 40) so that the active ingredient reaches the inflamed portion of the bowel at a sufficient concentration to exert its local action (col 4, ln 44 – 49). The coatings may optionally comprise plasticizers or release agents (anti-adhesives; col 5, ln 48 – 51).

Ulmius et al. does not discloses a combination of EUDRAGIT® NE 30 D with a polymer recited in subitem c) of claim 1, such as EUDRAGIT® FS.

Gang et al. discloses a colon specific delivery system which consists of a tablet core and double coating film (p 165, abstract), which has both a pH-dependent and time-dependent release mechanisms (p 165, ¶ 1 of introduction). The tablet was coated with EUDRAGIT® NE 30D as the inner coating and an outer, pH-dependent coating of EUDRAGIT® FS that degrades specifically in the colon (p 165, ¶ 3 of introduction). No plasticizers were used in the coating of the tablets (p 166, “Materials” and "Coating of tablets”). A 5.5% coating level for the EUDRAGIT® NE 30D resulted in colon-specific release (p 168), allowing for oral colon-specific drug delivery (p 169).

It would have been obvious to the person of ordinary skill in the art at the time the invention was made to prepare a dosage form as described by Ulmius et al. for the treatment of inflammatory bowel diseases using the coating system of Gang et al. The person of ordinary skill in the art would have been motivated to make those modifications to provide colon-specific delivery of the active ingredient following oral administration and reasonably would have expected success because Gang et al. disclose that an dual layer coating of EUDRAGIT® NE 30D and EUDRAGIT® FS results in the colon-specific delivery of active ingredient following oral administration. Such a dosage form would provide the active ingredient to the inflamed colon to exert a local effect. Gang et al. teaches that plasticizers and release agents are not required when this combination of polymer layers is used. The placement of the active ingredient can either be in a core, as disclosed by both Ulmius et al. and Gang et al., or in the inner polymeric layer as taught by Ulmius et al. (col 5, ln 5 – 12).

Gang et al. uses the same inner and outer (meth)acrylate copolymers as recited in the instant claims. Therefore, the dosage form must have the same percentage release of active substances in a hypotonic and isotonic release medium as both the cited prior and the instant claims recite dosage forms with the same structure. Dosage forms with the same layers must have the same physical properties, in this case, percentage release of active substance.

Conclusion

6. Applicant's submission of an information disclosure statement under 37 CFR 1.97(c) with the fee set forth in 37 CFR 1.17(p) on July 23, 2009 prompted the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 609.04(b). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Nissa M. Westerberg whose telephone number is (571)270-3532. The examiner can normally be reached on M - F, 8:00 a.m. - 4 p.m. ET.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Michael G. Hartley can be reached on (571) 272-0616. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Jake M. Vu/
Primary Examiner, Art Unit 1618

NMW